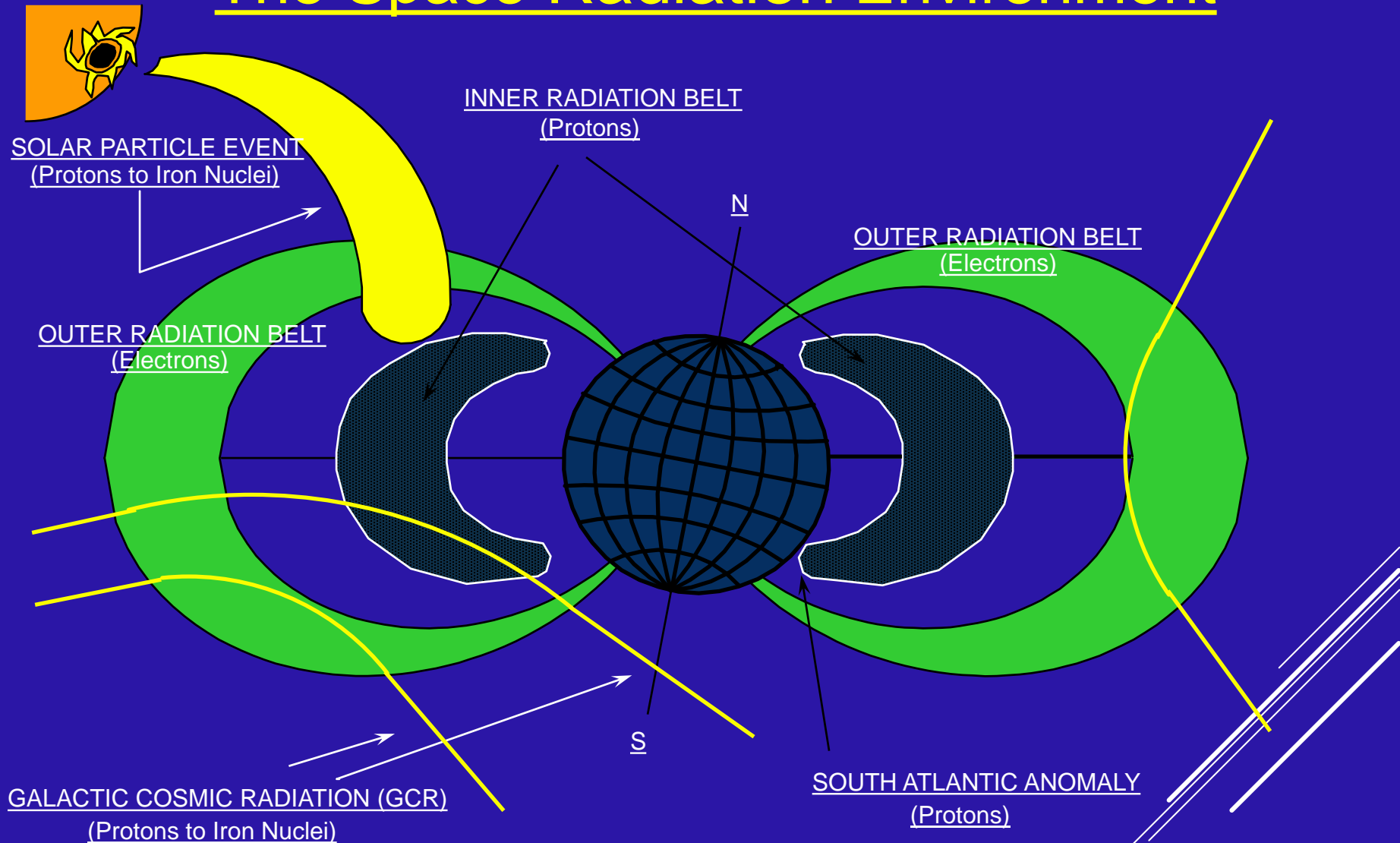


Detection of DNA Damage by Space Radiation in Human Fibroblast Cells Flown on the International Space Station

Honglu Wu
NASA Johnson Space Center
Houston, Texas, USA

The Space Radiation Environment



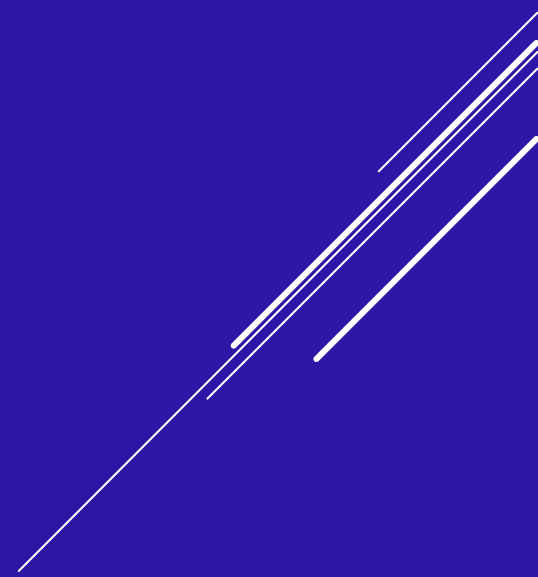
Space radiation : Energetic charged particles, high-LET (linear energy transfer)

Space Radiation Risks

- **Carcinogenesis (morbidity and mortality risk)**
- **Acute and Late Central Nervous System (CNS) risks**
 - ✓ immediate or late functional changes
- **Chronic & Degenerative Tissue Risks**
 - ✓ cataracts, heart-disease, etc.
- **Acute Radiation Risks** – sickness or death



WHAT ARE THE EVIDENT BIOLOGICAL EFFECTS OF SPACE RADIATION IN ASTRONAUTS?



LIGHT FLASHES

LIGHT FLASH FORMS

SHORT STREAK



STAR
(Single light point)



LONG STREAK
(Thin line of light)



DOUBLE STAR
(Double light points)



HOT DOG
(Wide line of light)



TADPOLE
(Tear drop shaped)



DOUBLE STREAK



CLOUD
(Diffuse)



SUPERNOVA
(Very bright flash)



SNOW
(More than
five short streaks)



CATARACTS

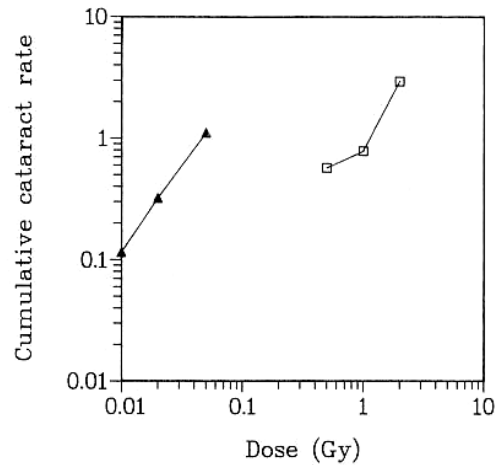
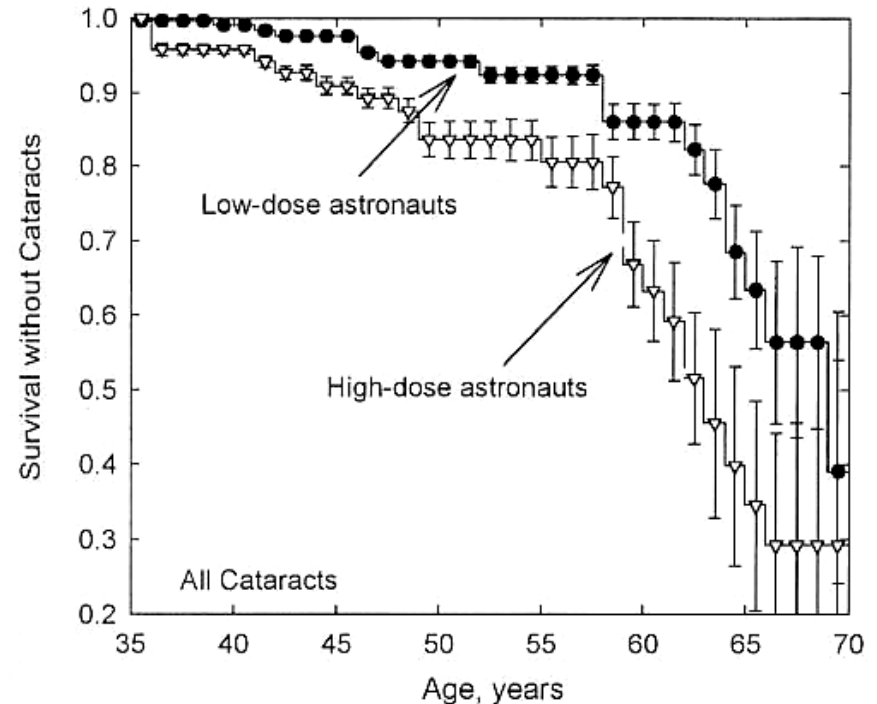


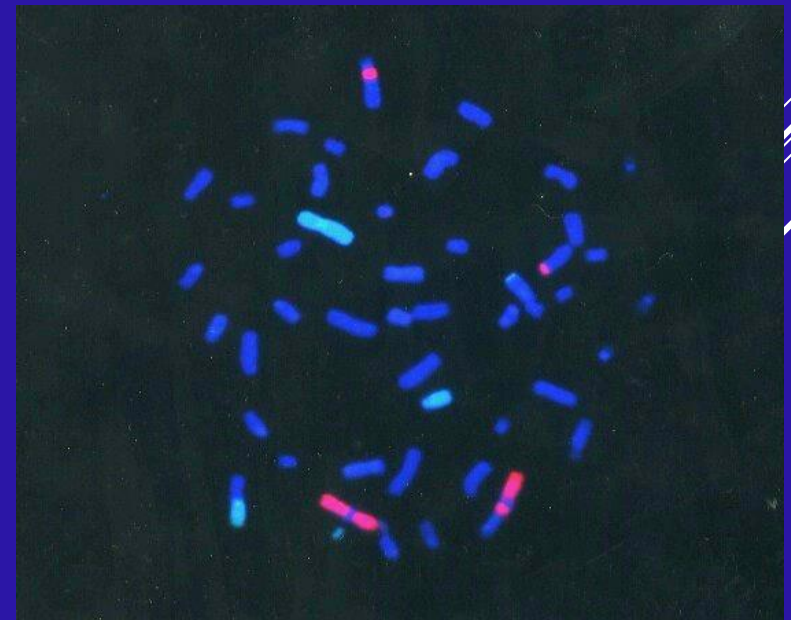
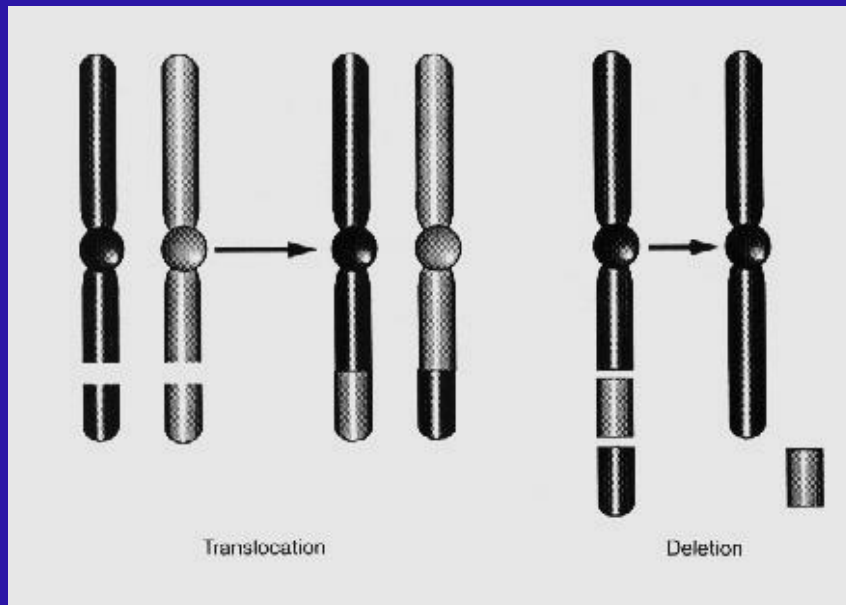
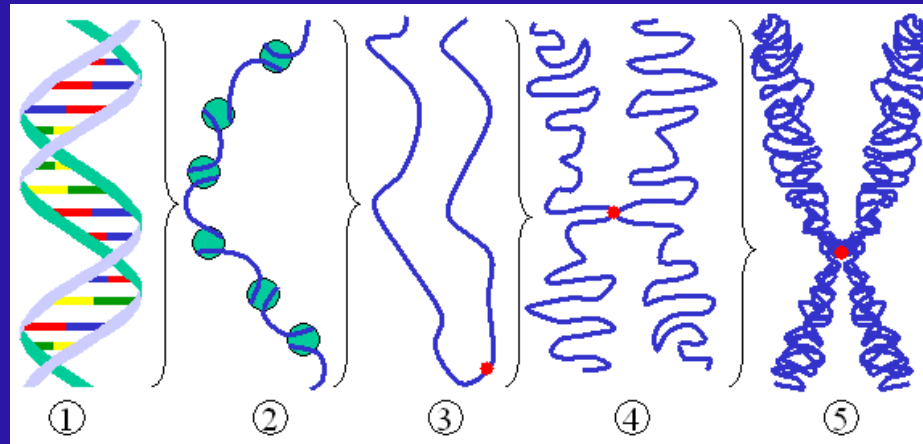
FIG. 2. Cumulative cataract rates (see text) for cataracts of grade 2 at 67 weeks postirradiation. \square , X rays; \blacktriangle , iron ions. The lines joining the points are to guide the eye only.

Brenner et al. Rad. Res. 1993



Cucinotta et al. 2001

CHROMOSOME ABERRATIONS OBSERVED IN ASTRONAUTS' LYMPHOCYTES



MicroRNA Expression Profile and DNA Damage Response in Cultured Human Fibroblasts in Space

Micro-7 Flight Experiment

(Funded by the NASA Fundamental Space Biology Program)



Objectives

Aim #1. Investigate changes of miRNA and RNA expression in G1 human fibroblast cells in space.

Aim #2. Investigate cellular responses to bleomycin-induced DNA damage in G1 human fibroblast cells in space.

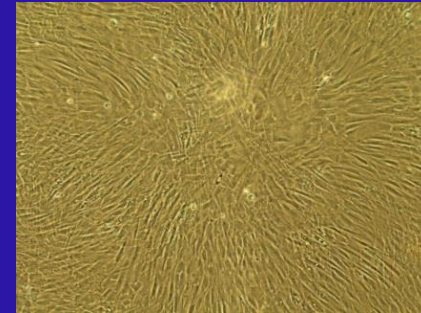
Aim #3. Detect the DNA damage in cells from direct exposure to space radiation.

A series of white lines of varying lengths and orientations are positioned in the bottom right corner of the slide, creating a decorative graphic element.

CELL CULTURE AND FLIGHT HARDWARE

Confluent human fibroblast cells were cultured in BioCells. The cells were kept in CGBA on ISS at 37 C.

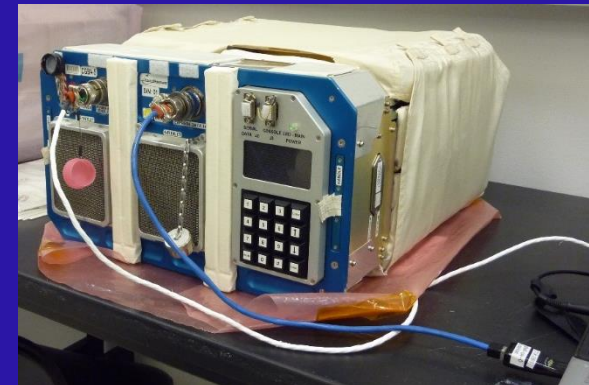
Human fibroblast cells



BioCell from BioServe



BioServe's CGBA incubator



Flight Schedule

4/18/14 – Cells were launched to ISS on board SpaceX-3.

4/22/14 – Cells were transferred to a 37 C incubator.

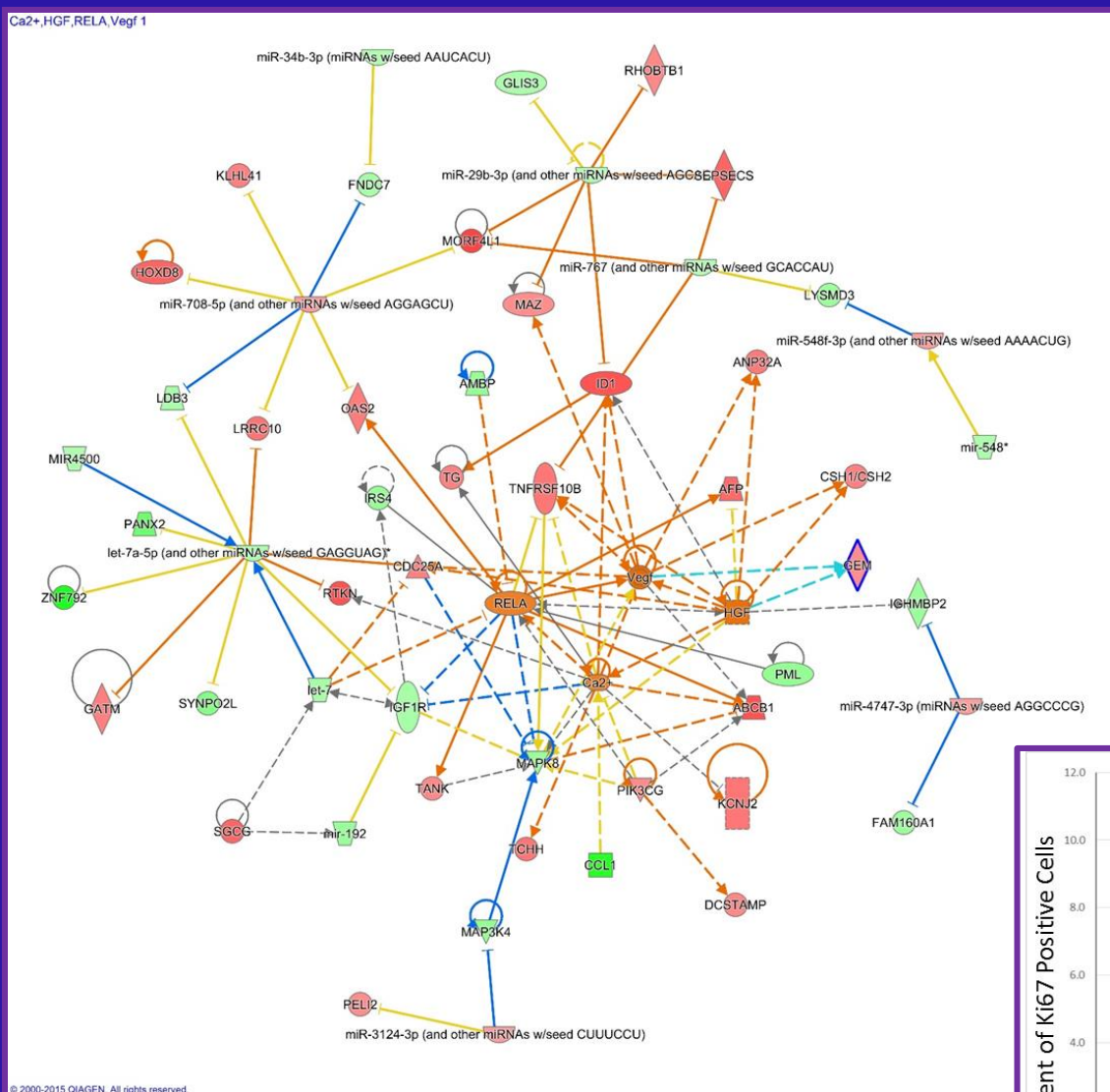
4/25/14 – Cells were fixed PFA (Day 3).

5/6/14 – Cells were fixed PFA (Day 14).

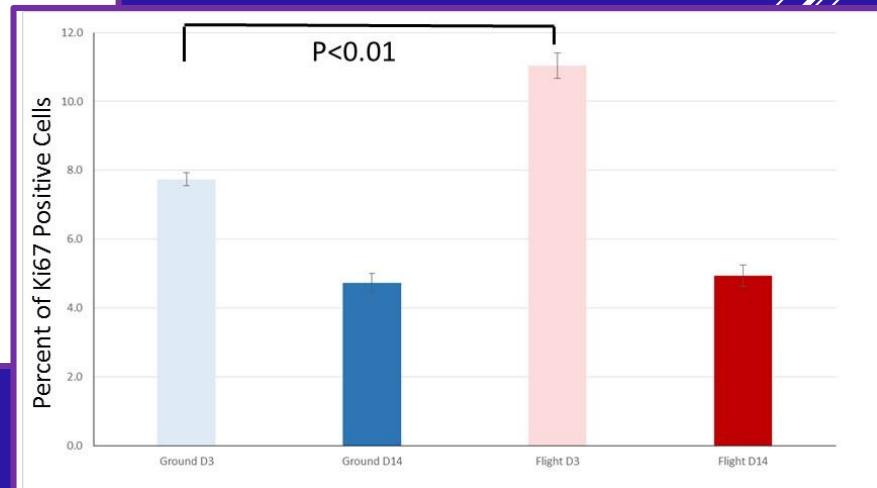
5/20/14 – The fixed samples returned to JSC.



RNA/miRNA expressions on Day 3 – Flight vs. ground

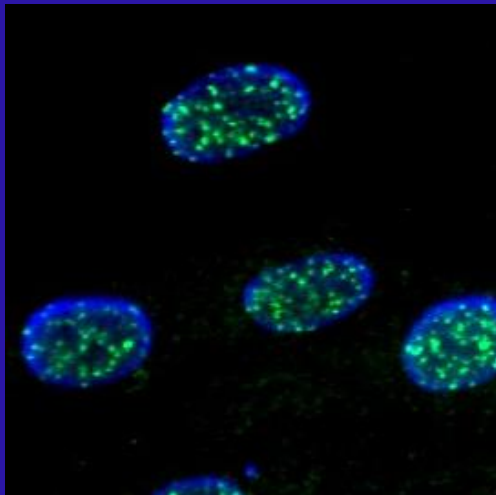


- The Day 3 data indicated activation of NF κ B and other growth related pathways involving HGF and VEGF in the flown cells.
- The results are consistent with faster cell proliferation of the cells in space as measured by the percentage of ki-67 positive cells.

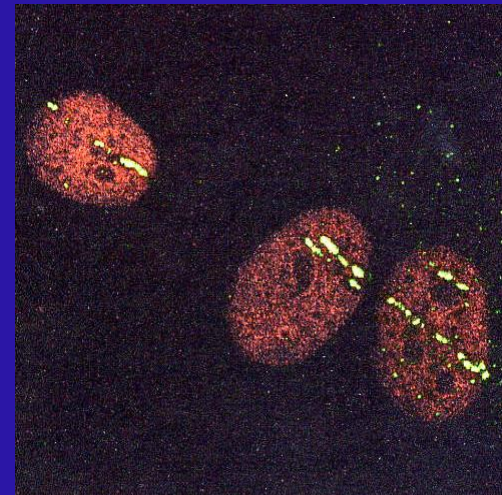


γ -H2AX as marker for DNA double strand breaks

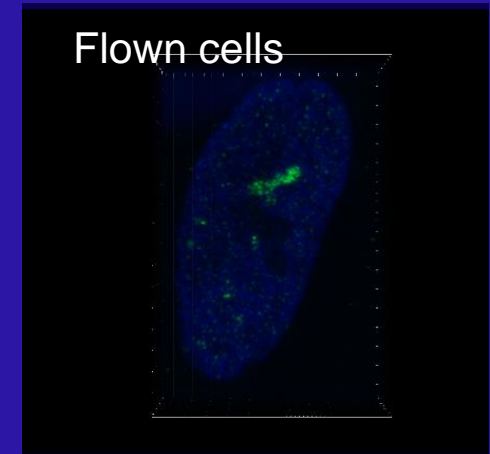
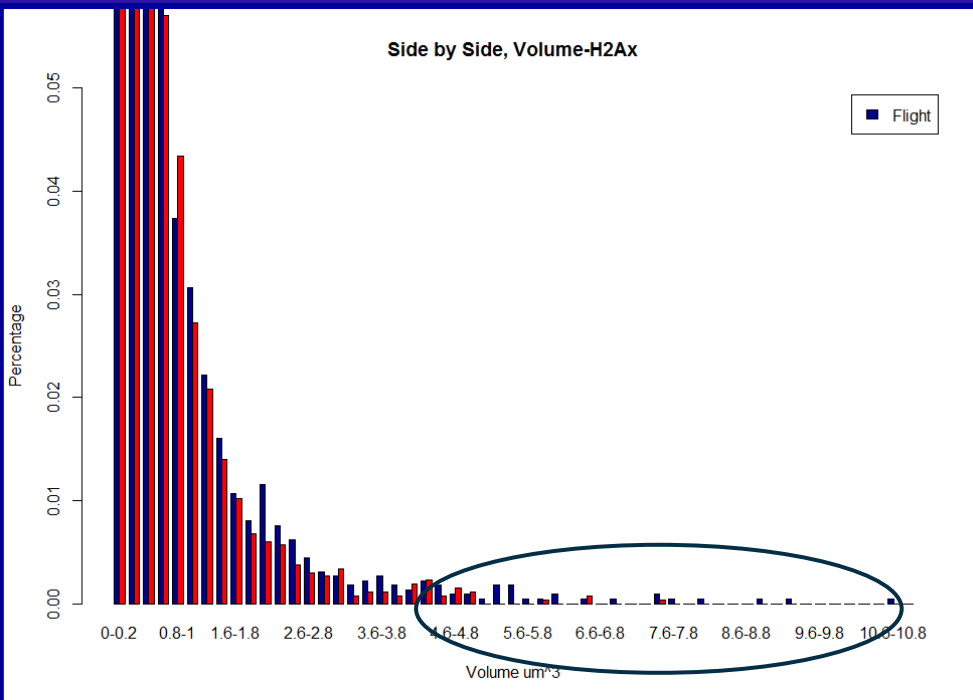
Low-LET
X-rays
Gamma rays



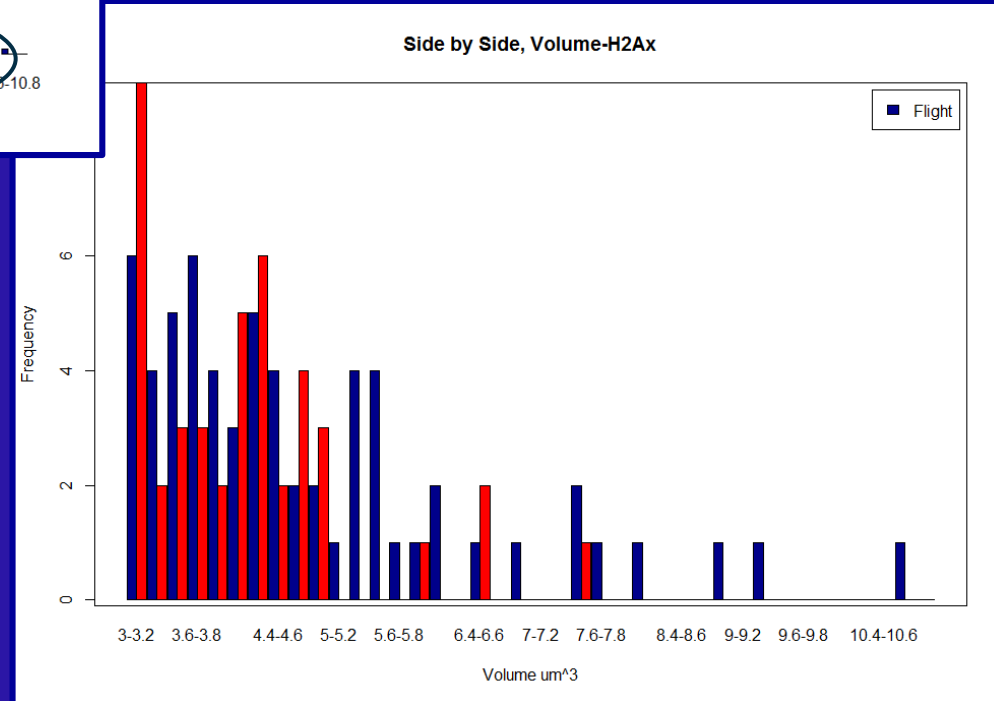
High-LET
Space radiation



Distribution of γ -H2AX foci size in flown cells

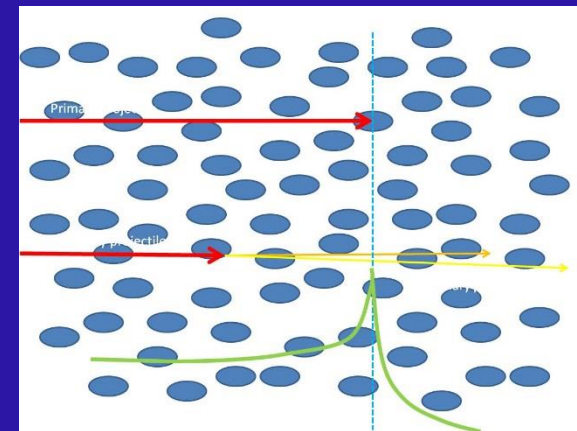
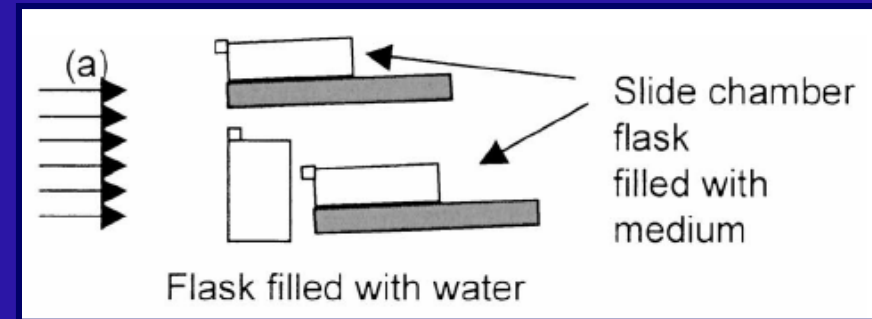
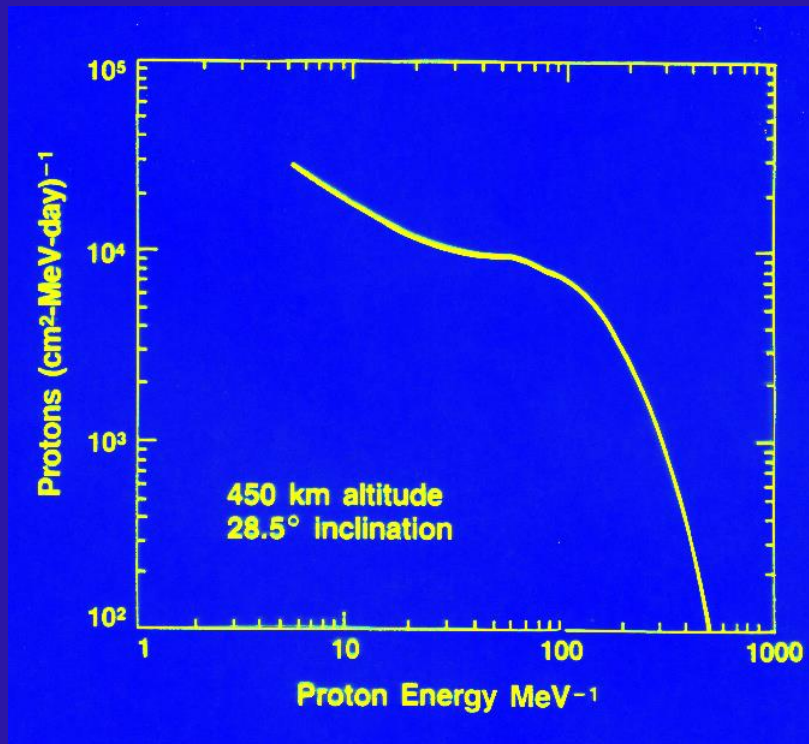


A small fraction of γ -H2AX foci are large and display a non-spherical track structure.



Low- and high-LET protons in LEO

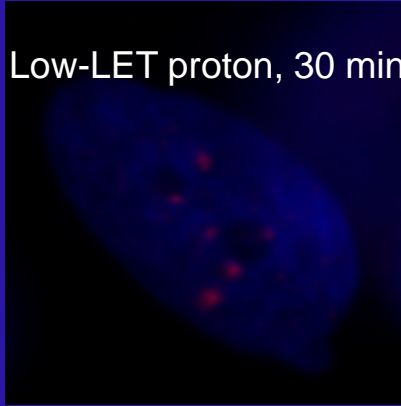
Energy spectrum of trapped protons



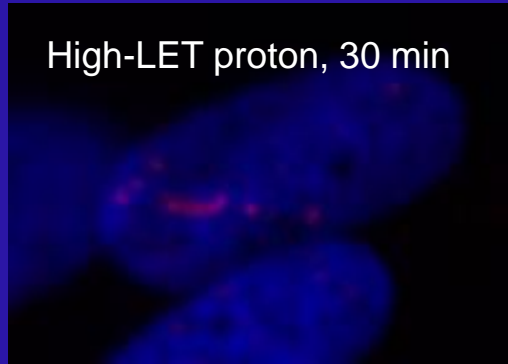
Bragg curve of protons

γ -H2AX foci induced by charged particles

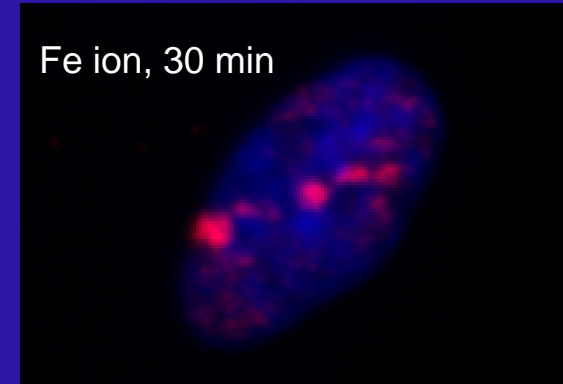
Low-LET proton, 30 min



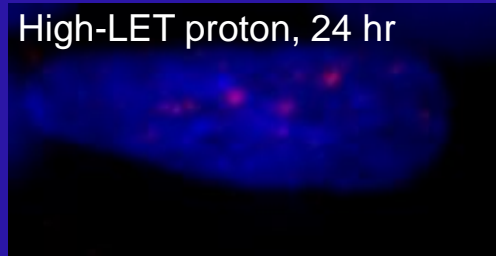
High-LET proton, 30 min



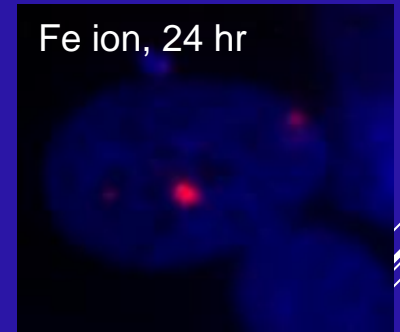
Fe ion, 30 min



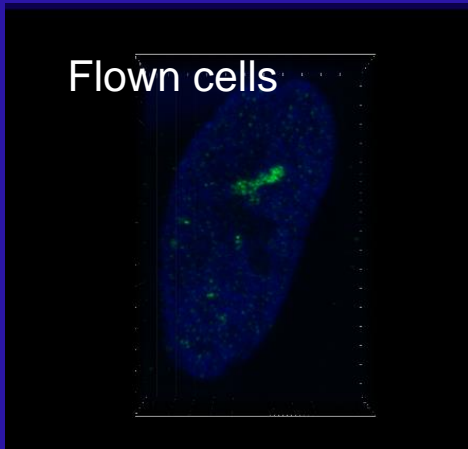
High-LET proton, 24 hr



Fe ion, 24 hr

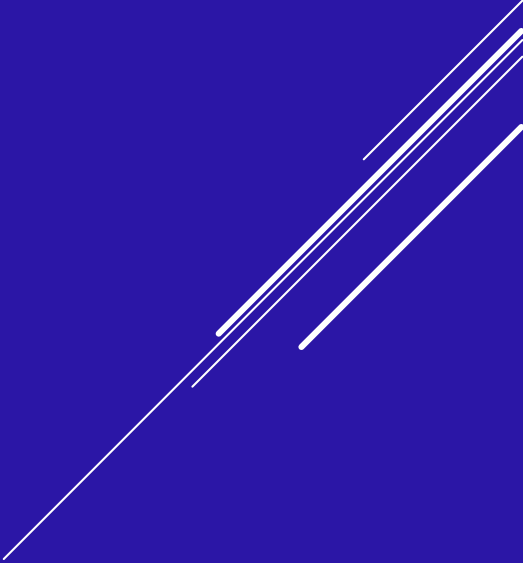


Flown cells



γ -H2AX tracks found in flight samples were most likely induced by high-LET protons or high-LET lighter ions

Conclusions

- A small fraction of large size foci were found in the cells flown in space in comparison to the ground controls, indicating that these foci were induced from exposure to space radiation.
 - Some of the foci had a clear track shape and were consistent with the foci induced by high-LET protons and Fe ions in the cells on the ground.
- 

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